§ 449.50 Nystatin.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Nystatin is the yellow to light-tan compound of a kind of nystatin or a mixture of two or more such compounds. It is very slightly soluble in water, moderately soluble in methyl alcohol, butyl alcohol, or propyl alcohol. It is so purified and dried that:

(i) Its potency is not less than 4,400 units of nystatin per milligram; except, if it is packaged for extemporaneous preparation of oral suspensions, its potency is not less than 5,000 units of nystatin per milligram.

(ii) [Reserved]

(iii) Its loss on drying is not more than 5.0 percent.

(iv) Its pH in a 3 percent aqueous suspension is not less than 6.5 and not more than 8.0.

(v) It passes the identity test.

(vi) If it is packaged for extemporaneous preparation of oral suspensions, it passes the suspendibility test.

(vii) If it is packaged for extemporaneous preparation of oral suspensions, it is crystalline.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5(b) of this chapter.

(3) *Requests for certification; samples.* In addition to the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, loss on drying, pH, and identity. In addition, if it is packaged for extemporaneous preparation of oral suspensions, results of tests and assays on the batch for suspendibility and crystallinity.

(ii) Samples required on the batch: 10 packages, each containing approximately 300 milligrams.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample in sufficient dimethylformamide to give a nystatin concentration of 400 units per milliliter (estimated). Further dilute with 10 percent potassium phosphate buffer, pH 6.0 (solution 6), to the reference concentration of 20 units of nystatin per milliliter (estimated).

(2) [Reserved]

(3) *Loss on drying.* Proceed as directed in § 436.200(b) of this chapter.

(4) *pH.* Proceed as directed in § 436.202 of this chapter, using a 3 percent aqueous suspension of the drug.

(5) *Identity.* Weigh approximately 100 milligrams of the sample into a 200-milliliter, glass-stoppered, volumetric flask. Add 50 milliliters of absolute methyl alcohol and 10 milliliters of glacial acetic acid. When the sample has dissolved, dilute to volume with methyl alcohol. Transfer 2 milliliters of this solution to a 100-milliliter volumetric flask and dilute to volume with methyl alcohol. Use the same dilution of acetic acid in methyl alcohol as the blank. Immediately determine the absorption peaks at 230, 291, 305, and 319 nanometers, and the shoulders at 279±2 nanometers, using a suitable ultraviolet spectrophotometer and quartz cells. Set the instrument to 100 percent transmission with the blank. If a recording spectrophotometer is used, record the ultraviolet absorption spectrum from 220 nanometers to 350 nanometers. If a nonrecording spectrophotometer is used, the exact positions of the peaks and shoulder should be determined for the particular instrument used. The ratio of the two absorbances

$$(A_{230}/A_{279})$$

should be not less than 0.90 and not more than 1.25.

(6) *Suspendibility test.* Transfer 200 milligrams of the sample into a 250-milliliter beaker containing 200 milliliters of water. Swirl the suspension gently with a stirring rod. Allow the beaker to remain still for 2 minutes and observe the bottom. It passes the test if the powder remains in suspension. If a significant amount of sediment is observed, withdraw an accurately measured aliquot of the undisturbed suspension and assay as directed in § 449.150c(b)(1) of this chapter. It passes the test if the suspension contains not less than 90 percent of the number of units of nystatin that it is represented to contain.

(7) *Crystallinity.* Proceed as directed in § 436.203(a) of this chapter.

[39 FR 19134, May 30, 1974, as amended at 39 FR 43833, Dec. 19, 1974; 49 FR 5098, Feb. 10, 1984; 50 FR 19920, May 13, 1985]